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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,865	02/27/2004	Dirk Gretzke	DEAV2003/0018 US NP	9913

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EXAMINER	
LEE, SUSANNAH E	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 08/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,865	GRETZKE ET AL.	
	Examiner	Art Unit	
	Susannah Lee	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5-9,11 and 12* is/are allowed.

6)☒ Claim(s) *1-4,10 and 13-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *NONE*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *082105* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

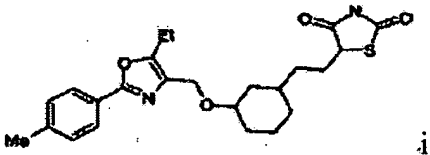
Claims 1-19 are pending in the instant application.

Priority

This application claims benefit of U.S. Provisional Application No. 60/487,432 filed on 07/15/2003.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) by application no. 10308354.5 filed in the German Patent Office on 02/27/2003, which papers have been placed of record in the file. The application names an inventor or inventors named in the prior application.

Response to Election/Restrictions

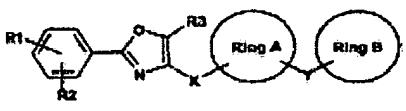
Applicant's election *without traverse* of Group I drawn to the compounds and compositions of formula (I), in the reply filed on 06/21/2005 is acknowledged. In addition, the election of species of Example XLIII,  is acknowledged. Based upon the election, examiner will begin searching the definitions of the compound of formula (I) as stated in the Response.

Scope of the Elected Invention

Claims 1-19 are pending in this application.

The scope of the elected subject matter that will be examined and searched is as follows:

Compounds, compositions, and methods of use of formula (I),



, depicted in claim 1, wherein:

Ring A is (C3-C8)-cycloalkanediyl;

Ring B is as stated in the reply on page 2;

R1, R2 are each independently H or (C1-C6)-alkyl;

R3 is (C1-C6)-alkyl;

X is as stated in the reply on page 2;

Y is (C1-C6)-alkanediyl.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The following terms of Claim 1 are not defined in the specification so as to know the structures of the compounds that are included and/or excluded by the term: "(C3-C8)-cycloalkanediyl" and "(C9-C11)-heteroaryl ring". Therefore, the specification lacks adequate support for Claim 1.

In addition, claims 1-4 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification although enabling for "(C6)-cycloalkanediyl" (Specification, Table 1, p. 33), it is not enabling to make or use the vast number of other potential "(C3-C8)-cycloalkanediyl" and

"(C9-C11)-heteroaryl ring" derivatives of the compounds of formula (I) of claim 1 without an undue amount of experimentation for the reasons described below.

As stated in MPEP 2164.01(a), "there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

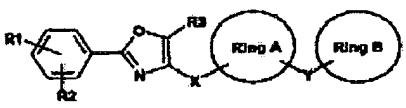
The factors to be considered when determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, were described in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as:

1. the nature of the invention;
2. the breadth of the claims;
3. the state of the prior art;
4. the relative skill of those in the art;
5. the predictability or unpredictability of the art;
6. the amount of direction or guidance presented (by the inventor);
7. the presence or absence of working examples; and
8. the quantity of experimentation necessary (to make and/or use the invention).

The eight Wands factors are applied to Claim 1 of the present invention below:

(1) The Nature of the Invention

The nature of the invention is a compound of the formula,



depicted in claims 1-4, wherein: **Ring A** is (C3-C8)-cycloalkanediyl; **Ring B** is as stated in the reply on page 2; **R1, R2** are each independently H or

(C1-C6)-alkyl; **R3** is (C1-C6)-alkyl; **X** is as stated in the reply on page 2; **Y** is (C1-C6)-alkanediyl.

(2) The Breadth of the claims

The breadth of Claims 1-4 encompass products of all "(C3-C8)-cycloalkanediyl" and "(C9-C11)-heteroaryl ring" derivatives of the compounds of formula (I) of claim 1. However, Claims 1-8 do not recite a chemical structure (or written equivalent) which expressly defines the "(C3-C8)-cycloalkanediyl" and "(C9-C11)-heteroaryl ring" derivatives, except for C6-cycloakanediyl.

The claims do not specify or enumerate which of the many types of "(C3-C8)-cycloalkanediyl" and "(C9-C11)-heteroaryl ring" derivatives which may contain a great number of ring sizes, from three membered rings to eight membered rings that fall within its scope. In addition the term heteroaryl is not further defined so as to know how many hetero atoms will be in the nine to eleven membered fused heterocyclic ring. The applicable rule for interpreting the claims is that "each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." See MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). In view of this rule, the products of Claims 1-4 may reasonably be interpreted to encompass *all* "(C3-C8)-cycloalkanediyl" and "(C9-C11)-heteroaryl ring" derivatives, which may contain any number of heteroatoms, as neither the claims nor the specification limit or define the products to a closed set of products.

(3) The state of the prior art

Certain azolidinediones, which exhibit similar antihyperglycemic activity have been described in U.S. Patent Numbers 5,468,762 and 5,532,256. In addition, the following journal articles describe similar compounds: Malamas et al., J. Med. Chem., 2000, 43, 995-1010 and Momose et al., J. Med. Chem., 2002, 45, 1518-1534.

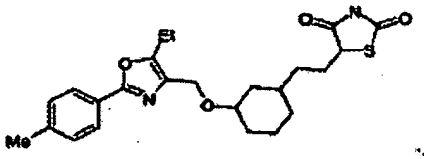
(4) The relative skill of those in the art

The level of skill in the art (pharmaceutical chemists, physicians) would be high.

(5) The predictability or unpredictability of the art

As demonstrated earlier, the compound claimed in the instant application, where the variables of **Ring A** and **R1** and **R2** could be "(C3-C8)-cycloalkanediyl" and "(C9-C11)-heteroaryl ring" derivatives include an extremely large scope of the potential products as encompassed by Claims 1-4 rendering the prior art unpredictable for making or using products as claimed on such a grand scale.

(6) The amount of direction or guidance presented (by the inventor)

The specification in the present invention discloses chemical examples of the species of preferred compounds, where Ring A is always C6-cycloalkanediyl and there are no (C9-C11)-heteroaryl ring systems in the examples provided in the specification, the elected species is an exemplary compound that is enabled, 

(7) The presence or absence of working examples

As noted in the previous section, the specification discloses the general role of the compound of claim 1. However, the specification has no working examples of where Ring A is anything but C6-cycloalkanediyl and where R1 or R2 can be a heteroaryl ring.

(8) The quantity of experimentation necessary (to make and/or use the invention)

Given the absence of direction or guidance (or working examples) in the specification for any of the extremely large number of compounds that would be encompassed by the descriptions "(C3-C8)-cycloalkanediyl" and "(C9-C11)-heteroaryl ring" it would cause a skilled artisan an undue amount of experimentation to determine which product the process of making was describing. Also, a skilled artisan would not be able to predict which "(C3-C8)-cycloalkanediyl" and "(C9-C11)-heteroaryl ring" compounds would be useful in treating the same disorders as the instant compound.

Applicant may overcome this rejection by pointing out where in the specification the terms are defined or by deleting the undefined terms.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims, for the reasons describe below.

As stated in MPEP 2164.01(a), "there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

The factors to be considered when determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, were described in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as:

1. the nature of the invention;
2. the breadth of the claims;
3. the state of the prior art;
4. the relative skill of those in the art;
5. the predictability or unpredictability of the art;
6. the amount of direction or guidance presented [by the inventor];
7. the presence or absence of working examples; and
8. the quantity of experimentation necessary [to make and/or use the invention].

The eight Wands factors are applied to Claim 16 of the present invention below:

(1) The Nature of the Invention

Claims 13-19 disclose methods of treating and preventing disorders from fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases.

(2) The Breadth of the claims

Claims 13-19 are directed to methods of treating and preventing disorders from fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases using products comprising a compound of formula (I) as defined by claim 1.

Claims 13-19 will be given its broadest reasonable interpretation. The applicable rule for interpreting the claims is that "each claim must be separately analyzed and given its broadest

reasonable interpretation in light of and consistent with the written description." See MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). In view of this rule, Claims 13-19, which does not specify the many possible types of disorders claimed will be interpreted to encompass all types of disorders claimed, which include fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases.

(3) The state of the prior art

It was known in the art at the time of this application that azolidinediones have antihyperglycemic properties, but the state of the art at the time of this application was that no single compound is known to treat all disorders from fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases. Applicant's specification does not provide support for treating all of these diseases.

(4) The relative skill of those in the art

The level of skill in the art (pharmaceutical chemists, physicians) would be high.

(5) The predictability or unpredictability of the art

It is noted that the pharmaceutical art generally is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement varies inversely with the degree of unpredictability in the factors involved. In re Fisher, 427 F.2d 833, 839. Therefore, the more unpredictable an area, the more specific enablement is needed in order to satisfy the statute. Added to the unpredictability of the art itself is the question whether without in vitro activity data, population data, and similar biological data

demonstrating the efficacy of the compound of formula (I) against fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases that the present invention could be reliably and predictably extrapolated to in vivo activity in patients with all types of fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases claimed. There is no absolute predictability, even in view of the high level of skill in the art.

(6) The amount of direction or guidance presented (by the inventor)

The specification in the present invention discloses on page 11 that there are several types of fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases, but there is insufficient guidance on the biological data in the specification for the role they play in all fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases.

(7) The presence or absence of working examples

As noted in the previous section, the specification discloses the general role of fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases. However, the specification has no working examples, such as in vivo or in vitro studies or patient population data of the role the compound of formula (I) of claim 1 plays in treating and preventing fatty acid metabolism, insulin resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases.

(8) The quantity of experimentation necessary (to make and/or use the invention)

Given the absence of direction or guidance (or working examples) in the specification for the role of the compound of formula (I) of claim 1 in treating fatty acid metabolism, insulin

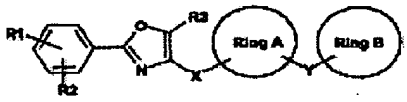
resistence, diabetes mellitus, dyslipidemia, squelae, and metabolic syndrome diseases, it would cause a skilled artisan an undue amount of experimentation to practice this invention to determine which patients with which diseases would benefit from which of the many claimed compounds within the scope of the invention with a reasonable expectation of success.

Applicant can overcome this rejection by deleting Claims 13-19.

A telephone interview was conducted with Attorney Barbara Kurys on 08/17/2005 to discuss the outstanding issues (please see enclosed interview summary form PTO-413).

Allowable Subject Matter

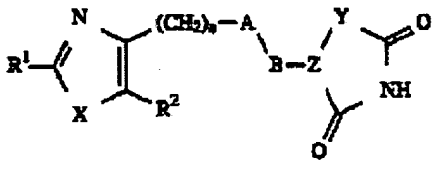
Claims 1-9 and 11-12 directed to compounds and compositions of formula (I),



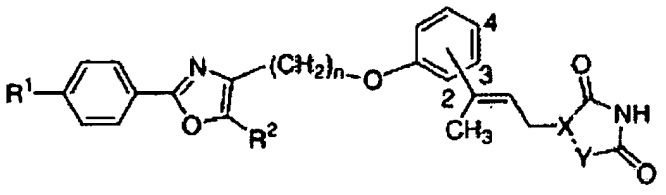
, depicted in claim 1, wherein **Ring A** is (C6)-cycloalkanediyl; **Ring B** is as stated in the reply on page 2; **R1, R2** are each independently H or (C1-C6)-alkyl; **R3** is (C1-C6)-alkyl; **X** is as stated in the reply on page 2; **Y** is (C1-C6)-alkanediyl are allowable over prior art of record at this point in the examination process.

Reasons for Allowance

The present invention is directed to Cycloalkyl derivatives having bioisosteric carboxylic acid groups and their pharmaceutical compositions. The closest prior arts of record are U.S. Pat. No. 5,468,762, which teach similar azolidinediones,



and a journal article by Malamas et al., titled "New Azolidinediones as Inhibitors of Protein Tyrosine Phophatase 1B with Antihyperglycemic Properties," J. Med. Chem., Vol. 43 (2000), pages 995-



1010, especially page 996, Compound 15,

Instead of a C6-cycloalkyl group at Ring A of the instant application, the prior art has a benzene ring.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Lee whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Date: 08/21/05